EXAMINER'S AMENDMENT

Prosecution on the merits of this application is re-opened.

A supplemental examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with David Parker on January 11, 2000.

The application has been amended as follows:

Claims 110-117 have been canceled without prejudice, and replaced with new claims 121-135.

~~121~~. A method for preparing a purified adenovirus composition comprising:

a) growing host cells in a serum-free media;

b) infecting said host cells with an adenovirus;

c) harvesting and lysing said host cells to provide a lysate comprising adenovirus; and

d) purifying adenovirus from said lysate by a process that includes a chromatography step without the use of cesium chloride density gradient centrifugation, wherein sad chromatography step involves a single chromatography step, to provide a purified adenovirus composition wherein the recovery of purified adenovirus after the chromatography step is 70% +/- 10% of the starting PFU.

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~~122~~. The method of claim ~~121~~, wherein said chromatography step involves ion exchange chromatography.

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~~123~~. The method of claim ~~122~~, wherein said ion exchange chromatography is anion exchange chromatography.

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~~124~~. The method of claim ~~123~~, wherein said anion exchange chromatography utilizes DEAE, TMAE, QAE, or PEI.

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~~125~~. The method of claim ~~123~~, wherein said anion exchange chromatography utilizes Toyopearl Super Q 650M, MonoQ, Source Q, or Fractogel TMAE.

D' cont. 76 71
~~126~~. The method of claim ~~121~~, wherein the adenovirus is subjected to purification steps that include reducing the concentration of contaminating nucleic acid.

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~~127~~. The method of claim ~~121~~, further defined as comprising the steps of concentrating said cell lysate, exchanging buffer of said cell lysate, and reducing the concentration of contaminating nucleic acids in said cell lysate.

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~~128~~. A method for preparing a purified adenovirus composition comprising:

a) growing host cells in a media;

b) infecting said host cells with an adenovirus;

c) harvesting and lysing said host cells to provide a lysate comprising adenovirus;

d) treating the lysate with a nuclease to reduce the concentration of contaminating nucleic acid; and

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e) purifying adenovirus from said lysate by a process that includes a chromatography step without the use of cesium chloride density gradient centrifugation, wherein sad chromatography step involves a single chromatography step, to provide a purified adenovirus composition wherein the recovery of purified adenovirus after the chromatography step is 70% +/- 10% of the starting PFU.

79 78
~~129~~. The method of claim ~~128~~, wherein said chromatography step involves ion exchange chromatography.

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~~130~~. The method of claim ~~129~~, wherein said ion exchange chromatography is anion exchange chromatography.

D' 81 80
und. ~~131~~. The method of claim ~~130~~, wherein said anion exchange chromatography utilizes DEAE, TMAE, QAE, or PEI.

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~~132~~. The method of claim ~~130~~, wherein said anion exchange chromatography utilizes Toyopearl Super Q 650M, MonoQ, Source Q, or Fractogel TMAE.

83 78
~~133~~. The method of claim ~~128~~, wherein the adenovirus is subjected to purification steps that include reducing the concentration of contaminating nucleic acid.

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~~134~~. The method of claim ~~128~~, further defined as comprising the steps of concentrating said cell lysate, and exchanging buffer of said cell lysate.

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~~135~~. The method of claim ~~128~~, wherein said media is serum-free media and the cells are capable of growing in serum-free media.

The following claims have also been added:

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70 ~~136~~. The method of claim ~~101~~ 61 wherein the lysing step d) uses hypotonic solution, hypertonic solution, impinging jet, microfluidization, solid shear, liquid shear, high pressure extrusion, or sonication.

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87 ~~137~~. The method of claim ~~118~~ 86 wherein the lysing step d) uses hypotonic solution, hypertonic solution, impinging jet, microfluidization, solid shear, liquid shear, high pressure extrusion, or sonication.

Examiner's comments

References B3 and C36 are cited as of interest (not available as prior art). The claims, as amended, are distinct from the disclosures of these references for the following reasons. References B3 and C36 do not teach or suggest feeding the adenovirus host cells by either fed-batch or perfusion methods as in required in claims 20, 70, 101, and 118, and do not teach or suggest the specific glucose levels recited in claim 70. Since the references teach harvesting virus from the culture supernatant after extended incubation, the references particularly teach away from use of perfusion, which is a process involving continual removal and replacement of culture supernatant. The references teach a purification process that completely removes contaminating serum albumin, and the references emphasize the elimination of enzymatic digestion steps; therefore the references provide no motivation to use a serum-free medium, as required by claim 121, and teach away from a nuclease treatment step as required by claim 128. The references do not teach or suggest lysing adenovirus host cells using a process that includes hypotonic solution,

hypertonic solution, impinging jet, microfluidization, solid shear, liquid shear, high pressure extrusion, or sonication, as required by new claims 136-137.

The claims have been renumbered for issue as follows:

Issue	Original	Issue	Original	Issue	Original	Issue	Original
1	20	24	29	47	87	69	109
2	2	25	30	48	89	70	136
3	22	26	53	49	90	71	121
4	23	27	56	50	91	72	122
5	24	28	54	51	92	73	123
6	25	29	55	52	93	74	124
7	26	30	70	53	94	75	125
8	27	31	71	54	95	76	126
9	3	32	72	55	96	77	127
10	4	33	73	56	97	78	128
11	5	34	74	57	88	79	129
12	6	35	80	58	98	80	130
13	7	36	81	59	99	81	131
14	13	37	82	60	100	82	132
15	14	38	75	61	101	83	133
16	15	39	76	62	102	84	134
17	8	40	77	63	103	85	135
18	9	41	78	64	104	86	118
19	10	42	79	65	105	87	137
20	11	43	83	66	106	88	119
21	12	44	84	67	107	89	120
22	21	45	85	68	108		
23	28	46	86				

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is (703) 308-2926. The

examiner can normally be reached on Monday -Thursday and alternate Fridays from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this Group is now (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, correspondence regarding this application should be directed to Group Art Unit 1641.

February 4, 2000

MARY E. MOSHER
PRIMARY EXAMINER
GROUP ~~1200~~ 1600